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Approach to the Febrile infant and child

Objectives

- Fever
- Ill looking child
- Occult bacteremia
- Sources of fever
- Sepsis vs SIRS
- Pathogens
- Work up
- Management
- Other DDX of Fever

Fever

- Clinically significant fever in children > 3 months .
- Measured Rectally a Temperature ≥ 38C is significant
- An ill appearing Child with fever warrants a detailed Hx &PE including vaccination, travel and animal contact
- Fever for > 7 days without a Focus is considered Fever of Unknown Origin (FUO)

Sources of Fever

Less Than 5 days duration

- Meningitis and meningioencephalitis
- Respiratory (upper and lower) most common source in all age groups
- Urinary tract infections common in infants < 3 months and children with risk factors
- Gastro intestinal infections common in formula fed infants and preschool children. This includes infectious Hepatitis.
- Skin and soft tissue infections
- Bone and joint infections

The Ill Febrile child

- How do we determine the “Ill” child ?

- General Exam is essential and depends on :
  - Level of consciousness and activity level
  - Presence of distress (Respiratory, agitation)
  - Abnormal Color (Central cyanosis, pallor, Jaundice)
  - Poor perfusion (mottling, Delayed CRT, weak pulses)
  - Hydration status (Skin turgor, sunken eyes, depressed fontanell, absent tears and no sweat, urine output)

The Ill Febrile child

- Vital signs
  - Temp.: infants and children may present with fever or hypothermia
  - HR: Usually tachycardic for age but may be bradycardic
    - < 12 months 160 beats/min
    - 1-2 years 150 beats/ min
    - 3-5 years 140 beats/ min
  - RR: Tachypnea, hypopnea or apnea
  - BP : Initially normal but later hypotension
    - Pt can be shocked with normal BP

The Ill Febrile Child

In an Ill appearing febrile child in addition to the usual vital signs and general exam always include

- Pulse oximetry (SaO_2)
- CRT (< 2 Sec)
- Blood glucose (> 40mg/dl in newborn, > 60 mg/dl in children)

	Green – low risk	Amber – intermediate risk	Red – high risk
Colour (of skin, lips or tongue)	• Normal colour	• Pallor reported by parent/carer	• Pale/mottled/ashen/ blue
Activity	• Responds normally to social cues • Content/smiles • Stays awake or awakens quickly • Strong normal cry/not crying	• Not responding normally to social cues • No smile • Wakes only with prolonged stimulation • Decreased activity	• No response to social cues • Appears ill to a healthcare professional • Does not wake or if roused does not stay awake • Weak, high-pitched or continuous cry
Respiratory		• Nasal flaring • Tachypnoea: – RR >50 breaths/ minute, age 6–12 months – RR >40 breaths/ minute, age >12 months • Oxygen saturation ≤95% in air • Crackles in the chest	• Grunting • Tachypnoea: RR >60 breaths/minute • Moderate or severe chest indrawing
Circulation and hydration	• Normal skin and eyes • Moist mucous membranes	• Tachycardia: – >160 beats/minute, age <12 months – >150 beats/minute, age 12–24 months – >140 beats/minute, age 2–5 years • CRT ≥3 seconds • Dry mucous membranes • Poor feeding in infants • Reduced urine output	• Reduced skin turgor
Other	• None of the amber or red symptoms or signs	• Age 3–6 months, temperature ≥39°C • Fever for ≥5 days • Rigors • Swelling of a limb or joint • Non-weight bearing limb/not using an extremity	• Age <3 months, temperature ≥38°C* • Non-blanching rash • Bulging fontanelle • Neck stiffness • Status epilepticus • Focal neurological signs • Focal seizures

Sepsis vs SIRS

Systemic inflammatory response syndrome : widespread inflammatory response that may or may not be associated with infection. The presence of two or more of the following criteria (one of which must be abnormal temperature or leukocyte count) defines SIRS

- Core temperature of >38.5°C or <36°C
- Tachycardia, defined as a mean heart rate more than two standard deviations above normal for age, or for children younger than one year of age, bradycardia defined as a mean heart rate <10th percentile for age
- Mean respiratory rate more than two standard deviations above normal for age or mechanical ventilation for an acute pulmonary process
- Leukocyte count elevated or depressed for age, or >10 percent immature neutrophils

Sepsis

Sepsis : The systemic inflammatory response syndrome in the presence of suspected or proven infection

- **Severe sepsis:** associated with cardiovascular dysfunction, or acute respiratory distress syndrome (ARDS), or dysfunction in two or more other organ systems as defined below
- **Septic shock**: sepsis with cardiovascular dysfunction
- **Refractory septic shock** : fluid-refractory septic shock and catecholamine-resistant septic shock

Sepsis
(Con't)

- **Multiple organ failure** :
  - **Cardiovascular** ;Hypotension, elevated arterial lactate, oliguria, or prolonged capillary refill.
  - **Respiratory** ; Hypoxia (on > 40%FiO_2), Hypercarbia, or need for mechanical ventilation
  - **Neurologic** ; Glasgow coma score ≤11 or acute change in mental status
  - **Hematologic**; Thrombocytopenia, disseminated intravascular coagulation (DIC)
  - **Renal**; Serum creatinine ≥2 times upper limit of normal for age or twofold increase in baseline creatinine
  - **Hepatic**; Total bilirubin ≥4 mg/dL (not applicable to newborn) or alanine aminotransferase (ALT) >2 times upper limit for age

Bacterial Pathogens

- *Staphylococcus aureus* including methicillin-resistant strains (MRSA)
- Coagulase-negative Staphylococcus especially in neonates or young infants with in-dwelling vascular catheters
- Streptococcus pneumoniae
- Group B streptococcus in the neonate
- Neisseria Meningitides
- Streptococcus pyogenes
- Heamophilus influenzae b
- *Pseudomonas aeruginosa* including carbapenem-resistant strains
- *Escherichia coli*, including those with extended spectrum beta-lactamase activity (ESBL)
- Klebsiella species, including those with ESBL activity

Viral Pathogens

- Influenza A &B
- Parainfluenza
- Adenovirus
- Respiratory Syncytial Virus (RSV)
- Human Metapneumovirus
- Coronavirus disease 2019 (COVID-19)
- Epstein-Barr virus (EBV)
- Cytomegalovirus (CMV)
- Herpes simplex virus (HSV)
- Enteroviruses

Other Pathogens

- Candida species
- Ricketsial infections (eg, Rocky Mountain spotted fever)

Occult Bacteremia

Occult bacteremia is defined as

The isolation of a bacterial pathogen in a blood culture taken from an otherwise well-appearing febrile child. The risk of occult bacteremia in these patients depends upon their immunization status

Occult Bacteremia

Before routine availability of PCV7 or PCV13 and Hib conjugate vaccines, the predominant pathogens were

- *S. pneumoniae* (80 %)
- Hib (20 %)
- *Neisseria meningitidis*
- *Staphylococcus aureus*
- group A beta-hemolytic *Streptococcus* [GABHS]
- group B *Streptococcus*
- *Salmonella* species
- *Escherichia coli*

Septic work up

- **White blood cell and absolute neutrophil counts**

ANC may be a better predictor of occult bacteremia in incompletely immunized children

- **Procalcitonin and other biomarkers**

PCT levels rise in response to bacterial infections more rapidly than other markers, such as C-reactive protein and ANC

PCT is more specific than WBC count

- **Cultures:** Blood, Urine, CSF, Sputum, any other body fluids
- **Molecular assays** : Molecular methods to identify bacterial infection include polymerase chain reaction (PCR) and detection of bacterial 16S ribosomal RNA genes or host RNA signatures.

Management

- ABC's
- Admit to floor vs PICU
- Fluids/ glucose &electrolytes
- Antimicrobials:
  - Infants below 90 days Cefotaxime or Amikacin + Ampiciline ± Acyclovir
  - Infants >90 days with no focus
    - Looking well : Ceftriaxone
    - Looking ill : Cephtriaxone + Vancomycin

Diagnostic criteria for Kawasaki disease

The diagnosis of KD requires the presence of fever lasting at least 5 days* without any other explanation combined with at least 4 of the 5 following criteria. A significant proportion of children with KD have a concurrent infection; therefore, ascribing the fever to such an infection or to KD requires clinical judgment.
Bilateral bulbar conjunctival injection
Oral mucous membrane changes, including injected or fissured lips, injected pharynx, or strawberry tongue
Peripheral extremity changes, including erythema of palms or soles, edema of hands or feet (acute phase), and periungual desquamation (convalescent phase)
Polymorphous rash
Cervical lymphadenopathy (at least 1 lymph node >1.5 cm in diameter)

KD: Kawasaki disease.

* If ≥4 of the above criteria are present, a diagnosis of KD can be made on day 4 of illness.

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WHO Case Definition of Multisystemic Inflammatory Syndrome in Children (MIS-C)

All 6 criteria must be present

1. Age 0 to 19 years
2. Fever for ≥3 days
3. Clinical signs of multisystem involvement (**at least 2** of the following):
   - Rash, bilateral nonpurulent conjunctivitis, or mucocutaneous inflammation signs (oral, hands, or feet)
   - Hypotension or shock
   - Cardiac dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiographic findings or elevated troponin/BNP)
   - Evidence of coagulopathy (prolonged PT or PTT; elevated D-dimer)
   - Acute gastrointestinal symptoms (diarrhea, vomiting, or abdominal pain)
4. Elevated markers of inflammation (eg, ESR, CRP, or procalcitonin)
5. No other obvious microbial cause of inflammation, including bacterial sepsis and staphylococcal/streptococcal toxic shock syndromes
6. Evidence of SARS-CoV-2 infection
   - **Any** of the following:
     - Positive SARS-CoV-2 RT-PCR
     - Positive serology
     - Positive antigen test
     - Contact with an individual with COVID-19